

## FIG. 1A

SEQ ID NO: 1

Nucleotide Sequence Tankyrase Homologue isotype1

CTTTGAAGACACTGGATTTTCATACTTTTGCCTGGGGTTATCTCTCTGTGTCTCACTACATAGACAAATA  
TTAGCTGTGAGCAGATCTTTTTTTGTTGCTTCTTGTAGTCCCCCAGTTTAGCAGAAACATTCTGTGAGA  
TAGATGTGGGAAAGGAATTCTAGCAAGAGTTTTGTCACTGTATCATAAGGTTGTGATTTACATATTTAA  
GTTTTATACTTTGAACATCTGAAAATGTATACATACTAAATATGCAGAACTCTATTGTAGAGTGAGAAA  
CATTTGAACTTTGAGCTTTTCACTCACTTATTTTGTATTCTTTCTTTGAGGTTAGCAGTAGTACCACCCA  
AGGCACTGCTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTTATCATTAAAGGTTTTGGGCG  
GAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAGTGTCCAAGCACGTGATGATGGGGGCCTTAT  
TCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCCTTTTGGCAGATGGTGCAGA  
CCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAATTAAAGGAAAGATTGATGT  
TTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAGATGGAAGGACAGCATTGGA  
TTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGTGC  
CAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATGTCAACTGCCACGCAAGTGA  
TGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAAAGATTGTACAGCTGTTACT  
GCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCATTACACAATGCCTGTTCTTA  
TGGTCATTATGAAGTAACTGAACTTTTTGGTCAAGCATGGTGCCTGTGTAAATGCAATGGACTTGTGGCA  
ATTCACCTCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTTCTCTTCTCTTAAGTTATGG  
TGCAGACCCAACACTGCTCAATTGTCACAATAAAAGTGCTATAGACTTGGCTCCCACACCACAGTTAAA  
AGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCG  
AATCAAAAAACATCTCTCTCTGGAAATGGTGAATTTCAAGCATCCTCAAACACATGAAACAGCATTGCA  
TTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAACTGTTGCTAAGAAAAGGAGCAAA  
CATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTGAGAAAGCTCATAATGATGT  
TGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATCTTGGTCAGACTTCTCTACA

CAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCTACTCCTGAGCTATGGGTGTGATCCTAACAT  
TATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTACAGCAACTCCTCCAAGAGGG  
TATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGATGTGCGAAAC  
TGTAaaaaaaactGTGTACTGTTcagAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCTACACCACT  
TCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGGAAATATCTGCTACAGCATGGAGCTGATGTGCA  
TGCTAAAGATAAAGGAGGCCTTGTACCTTGCACAATGCATGTTCTTATGGACATTATGAAGTTGCAGA  
ACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAATTTACACCTTTACATGAAGC  
AGCAGCAAAGGAAAATATGAAATTTGCAAACCTTCTGCTCCAGCATGGTGCAGACCCTACCAAAAAA  
CAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATATTCAAGATCTGCTTAGGGG  
AGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGAAGAAGTTGTCTTCTCCTGA  
TAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATTTAGCAGCTGGTTATAATAA  
TTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCAAGACAAAGGAGGACTTAT  
TCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTACTAATAAAGTATAATGCATG  
TGTCATGCCACGGACAAATGGGCTTTCACACCTTTCACGGAAGCAGCCCAAAAGGGACGAACACAGCT  
TTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGGAAGGACAAACACCTTTAGA  
TTTAGTTTCAGCGGATGATGTcAGCGCTCTTCTGACAGCAGCCATGCCCCATCTGCTCTGCCCTCTTG  
TTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCAGGAGCCACTGCAGATGCTCTCTCTTCAGGTCC  
ATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACCTTATCTGGGAGTTTTTCAGAACTGTC  
TTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAAGGAGGTTCCAGGAGTAGA  
TTTTAGCATAACTCAATTCGTAAGGAATCTTGGAAGTTGAGCACCTAATGGATATATTTGAGAGAGAACA  
GATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGG  
ACATAGGCACAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTTAACCCATATTT  
AACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTGATGATAAAGAGTTTCAGTC  
TGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCATGCAGGTGGAATCTTCAA  
CAGATACAATATTCTCAAGATTcAGAAGGTTTGTAAACAAGAACTATGGGAAAGATACACTCACCGGAG  
AAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTATTTTCATGGGTCTCCTTTTGT  
GAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTGGTATGTTTGGAGCTGGCAT  
TTATTTTGCTGAAAACCTTCCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCC  
AGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTTGCCGGGTAAACCTTGGGAAA  
GTCTTTCCTGCAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTCATCACTCAGTCACTGGTAG  
GCCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAGAACAGGCTTATCCTGAGTA  
TTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAATAGTTATTTTAAGAACTA  
ATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTACTCCTTTGCTGAAAAAAA  
AA

**FIG. 1B**

## FIG.\_2A

SEQ ID NO: 2

Nucleotide Sequence Tankyrase Homologue isotype2

CGCGCTGCTCCGCCCCGCCGCGGGGCAGCCGGGGGGCAGGGAGCCCAGCGAGGGGCGCGCGTGGGCGCGG  
CCCATGGGACTGCGCCGGATCCGGTGACAGCAGGGAGCCAAGCGGCCCGGGCCCTGAGCGCGTCTTCTC  
CGGGGGGCGCTCGCCCTCCTGCTCGCGGGGCCGGGGCTCCTGCTCCGGTTGCTGGCGCTGTTGCTGGCTG  
TGGCGGCGGGCCAGGATCATGTGCGGTCGCCGCTGCGCCGGCGGGGGAGCGGCCTGCGCGAGCGCCGCGG  
CCGAGGCCGTGGAGCCGGCCGCCGAGAGCTGTTTCGAGGCGTGCCGCAACGGGGACGTGGAACGAGTCA  
AGAGGCTGGTGACGCCTGAGAAGGTGAACAGCCGCGACACGGCGGGCAGGAAATCCACCCCGCTGCACT  
TCGCCGCAGGTTTTGGGCGGAAAGACGTAGTTGAATATTTGCTTCAGAATGGTGCAAATGTCCAAGCAC  
GTGATGATGGGGGCCTTATTCCTCTTCATAATGCATGCTCTTTTGGTCATGCTGAAGTAGTCAATCTCC  
TTTTGCGACATGGTGCAGACCCCAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAA  
TTAAAGGAAAGATTGATGTTTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCCGAAATACAG  
ATGGAAGGACAGCATTGGATTTAGCAGATCCATCTGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAG  
ATGAACTCTTAGAAAGTGCCAGGAGTGGCAATGAAGAAAAAATGATGGCTCTACTCACACCATTAAATG  
TCAACTGCCACGCAAGTGATGGCAGAAAGTCAACTCCATTACATTTGGCAGCAGGATATAACAGAGTAA  
AGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCAT  
TACACAATGCCTGTTCTTATGGTCATTATGAAGTAACTGAACTTTTGGTCAAGCATGGTGCCTGTGTAA  
ATGCAATGGACTTGTGGCAATTCCTCCTCTTCATGAGGCAGCTTCTAAGAACAGGGTTGAAGTATGTT  
CTCTTCTCTTAAGTTATGGTGCAGACCCCACTGCTCAATTGTACAATAAAAGTGCTATAGACTTGG  
CTCCACACCACAGTTAAAGAAAGATTAGCATATGAATTTAAAGGCCACTCGTTGCTGCAAGCTGCAC  
GAGAAGCTGATGTTACTCGAATCAAAAAACATCTCTCTTGGAATGGTGAATTTCAAGCATCCTCAAA  
CACATGAAACAGCATTGCATTGTGCTGCTGCATCTCCATATCCCAAAGAAAGCAAATATGTGAACTGT  
TGCTAAGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTG  
AGAAAGCTCATAATGATGTTGTTGAAGTAGTGGTGAAACATGAAGCAAAGGTTAATGCTCTGGATAATC

TTGGTCAGACTTCTCTACACAGAGCTGCATATTGTGGTCATCTACAAACCTGCCGCCTACTCCTGAGCT  
ATGGGTGTGATCCTAACATTATATCCCTTCAGGGCTTTACTGCTTTACAGATGGGAAATGAAAATGTAC  
AGCAACTCCTCCAAGAGGGTATCTCATTAGGTAATTCAGAGGCAGACAGACAATTGCTGGAAGCTGCAA  
AGGCTGGAGATGTGAACTGTAAAAAACTGTGTACTGTTTCAGAGTGTCAACTGCAGAGACATTGAAG  
GGCGTCAGTCTACACCACTTCATTTTGCAGCTGGGTATAACAGAGTGTCCGTGGTGAATATCTGCTAC  
AGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCTTGACCTTTGCACAATGCATGTTCTTATG  
GACATTATGAAGTTGCAGAACTTCTTGTTAAACATGGAGCAGTAGTTAATGTAGCTGATTTATGGAAAT  
TTACACCTTTACATGAAGCAGCAGCAAAAGGAAAATATGAAATTTGCAAACTTCTGCTCCAGCATGGTG  
CAGACCCTACCAAAAAAACAGGGATGGAAATACTCCTTTGGATCTTGTTAAAGATGGAGATACAGATA  
TTCAAGATCTGCTTAGGGGAGATGCAGCTTTGCTAGATGCTGCCAAGAAGGGTTGTTTAGCCAGAGTGA  
AGAAGTTGTCTCTCCTGATAATGTAAATTGCCGCGATACCCAAGGCAGACATTCAACACCTTTACATT  
TAGCAGCTGGTTATAATAATTTAGAAGTTGCAGAGTATTTGTTACAACACGGAGCTGATGTGAATGCCC  
AAGACAAAGGAGGACTTATTCCTTTACATAATGCAGCATCTTACGGGCATGTAGATGTAGCAGCTCTAC  
TAATAAAGTATAATGCATGTGTCAATGCCACGGACAAATGGGCTTTACACCTTTGCACGAAGCAGCCC  
AAAAGGGACGAACACAGCTTTGTGCTTTGTTGCTAGCCCATGGAGCTGACCCGACTCTTAAAAATCAGG  
AAGGACAAACACCTTTAGATTTAGTTTCAGCGGATGATGTCAGCGCTCTTCTGACAGCAGCCATGCCCC  
CATCTGCTCTGCCCTCTTGTTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGCCCAGGAGCCACTGCAG  
ATGCTCTCTCTTCAGGTCCATCTAGCCCATCAAGCCTTTCTGCAGCCAGCAGTCTTGACAACCTTATCTG  
GGAGTTTTTTCAGAACTGTCTTCAGTAGTTAGTTCAAGTGGAACAGAGGGTGCTTCCAGTTTGGAGAAAA  
AGGAGGTTCCAGGAGTAGATTTTAGCATAACTCAATTCGTAAGGAATCTTGGACTTGAGCACCTAATGG  
ATATATTTGAGAGAGAACAGATCACTTTGGATGTATTAGTTGAGATGGGGCACAAGGAGCTGAAGGAGA  
TTGGAATCAATGCTTATGGACATAGGCACAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAAC  
AAGGTCTTAACCCATATTTAACTTTGAACACCTCTGGTAGTGGAACAATTCTTATAGATCTGTCTCCTG  
ATGATAAAGAGTTTCAGTCTGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTC  
ATGCAGGTGGAATCTTCAACAGATACAATATTCTCAAGATTGAGAAGGTTTGTAAACAAGAACTATGGG  
AAAGATACACTCACCGGAGAAAAGAAGTTTCTGAAGAAAACCACAACCATGCCAATGAACGAATGCTAT  
TTCATGGGTCTCCTTTTGTGAATGCAATTATCCACAAAGGCTTTGATGAAAGGCATGCGTACATAGGTG  
GTATGTTTGGAGCTGGCATTATTTTGTGCTGAAAACCTTCCAAAAGCAATCAATATGTATATGGAATTG  
GAGGAGGTACTGGGTGTCCAGTTCACAAAGACAGATCTTGTTACATTTGCCACAGGCAGCTGCTCTTTT  
GCCGGGTAACCTTGGGAAAGTCTTTCCTGCAGTTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTC  
ATCACTCAGTCACTGGTAGGCCAGTGTAATGGCCTAGCATTAGCTGAATATGTTATTTACAGAGGAG  
AACAGGCTTATCCTGAGTATTTAATTACTTACCAGATTATGAGGCCTGAAGGTATGGTCGATGGATAAA  
TAGTTATTTTAAAGAACTAATTCCACTGAACCTAAATCATCAAAGCAGCAGTGGCCTCTACGTTTTAC  
TCCTTTGCTGAAAAA

**FIG.\_2B**

SEQ ID NO: 3

**Amino Acid Sequence Tankyrase Homologue isotype1**

GFGRKDVVEYLLQNGASVQARDDGGLIPLHNACSFGEVNVNLLLRHGADPNARDNWNYPPLHEAAIKG  
KIDVCIVLLQHGAEP TIRNTDGR TALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNVNC  
HASDGRKSTPLHLAAGYNRVKIVQLLLQH GADVHAKDKGDLVPLHNACSYGHYEVT ELLVKGHACVNAM  
DLWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKS AIDLAPTQ LKERLAYEFKGHSL LQAAREA  
DVTRIKKHL SLEMVNF KHPQTHETALHCAA SPYPKRKQICELL LRKGANINEKTKEFLT PLHVASEKA  
HNDVVEVVVKHEAKVNALDNLGQTS LHRAAYCGHLQTCRLLLSYGC DPNIISLQGFTALQMGNENVQQL  
LQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQH G  
ADVHAKDKGGLVPLHNACSYGHYEVAELLVKGHGVNVADLWKFTPLHEAAAKGKYEICKLLLQH GADP  
TKKNRDGNTPLDLVKDGD TDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHLAA  
GYNNLEVAEYLLQH GADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQKG  
RTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMP PSALPSCYKPQVLNGVRS PGATADAL  
SSGPSSPSSL SAASSLDNLSGSFSELSSVVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLM DIF  
EREQITLDVLVEMGHKELKEIGINAYGHRHKL IKGVERLISGQQGLNPYLTLNTSGSGTILIDLSPDDK  
EFQSVEEEMQSTVREHRDGGHAGGIFNRYN ILKIQKVCNKKLWERYTHRRKEVSEENHNHANERMLFHG  
SPFVNAI IHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQL LFCRV  
TLGKSFLQFSAMKMAHSPPGHHSVTGRPSV NGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDG

**FIG.\_3**

SEQ ID NO: 4

**Amino Acid Sequence Tankyrase Homologue isotype2**

RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQAARALSASSPGGLALLLAGPGLLLRLLALLLAV  
AAARIMSGRRRCAGGGAACASAAAEAVEPAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHF  
AAGFGRKDVVEYLLQNGANVQARDGGLIPLHNACSFHAEVNNLLRHGADPNARDNWNYPPLHEAAI  
KGKIDVCIVLLQHGAEP TIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNV  
NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHEVTELLVKHGACVN  
AMDWQFTPLHEAASKNRVEVCSLLLSYGADPTLLNCHNKSALDLAPTQPKERLAYEFKGHSLQAAAR  
EADVTRIKKHLSELMVNEFKHPQTHETALHCAAASPYPKRKQICELLRKGANINEKTKEFLTPLHVASE  
KAHNDVVEVVVKHEAKVNALDNLGQTS LHRAAYCGHLQTCRLLLSYGCDPNIISLQGFTALQMGNEENVQ  
QLLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQ  
HGADVHAKDKGGLVPLHNACSYGHEVAELLVKHGAVNVADLWKFTPLHEAAAKGKYEICKLLLQHGA  
DPTKKNRDGNTPLDLVKDGD TDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHL  
AAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQ  
KGRTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPSALPSCYKPQVLNGVRSFGATAD  
ALSSGPSSPSSLSAASSLDNLSGSFSELSSVVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLMD  
IFEREQITLDVLVEMGHKELKEIGINAYGHRHKLKIGVERLISGQGLNPYLTNTSGSGTILIDLSPD  
DKEFQSVEEEMQSTVREHRDGGHAGGIFNRYNLIKIQKVCNKKLWERYTHRRKEVSEENHNHANERMLF  
HGSPFVNAI IHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGIGGGTGCPVHKDRSCYICHRQLLFC  
RVTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDG

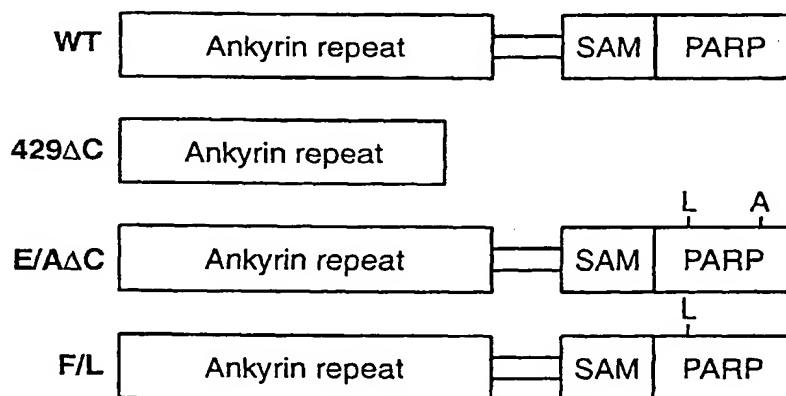
**FIG.\_4**

### Schematic Presentation of Dominant Negative Mutants for Tankyrase Homologue

#### Dominant Negative Mutants

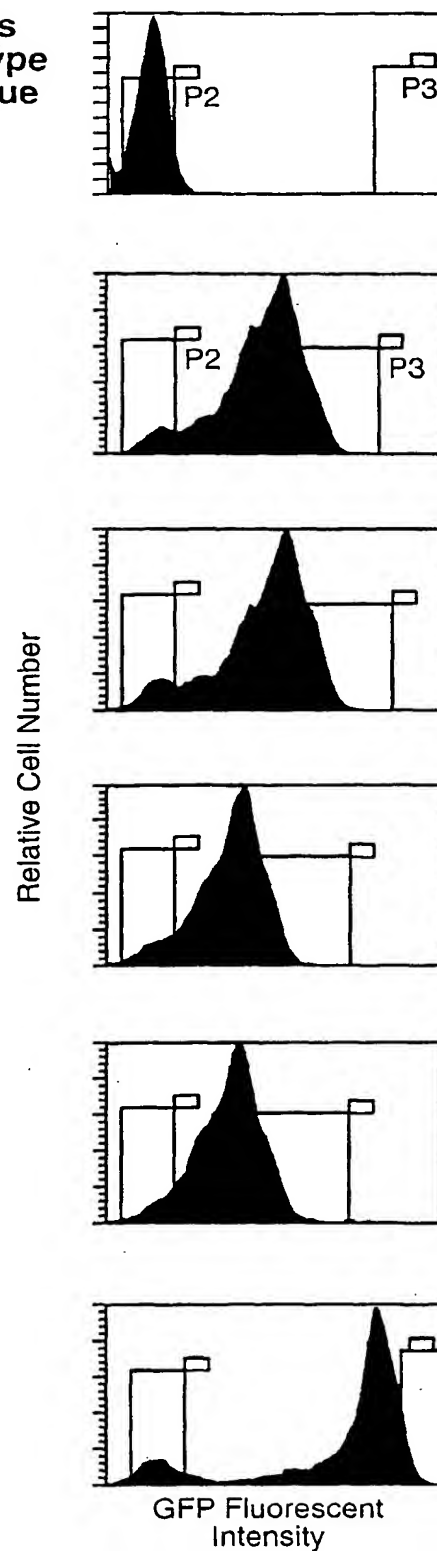
Truncation: 429 $\Delta$ C- of the C-terminal catalytic domain – truncation of the catalytic domain of PARP acts as a dominant negative when overexpressed *in vivo* (Oncogene 1999 Nov 25; 18(50):7010-5)

Point mutant: E945A $\Delta$ C- conserved residue in PARP domain, thought to be important in NAD<sup>+</sup> binding



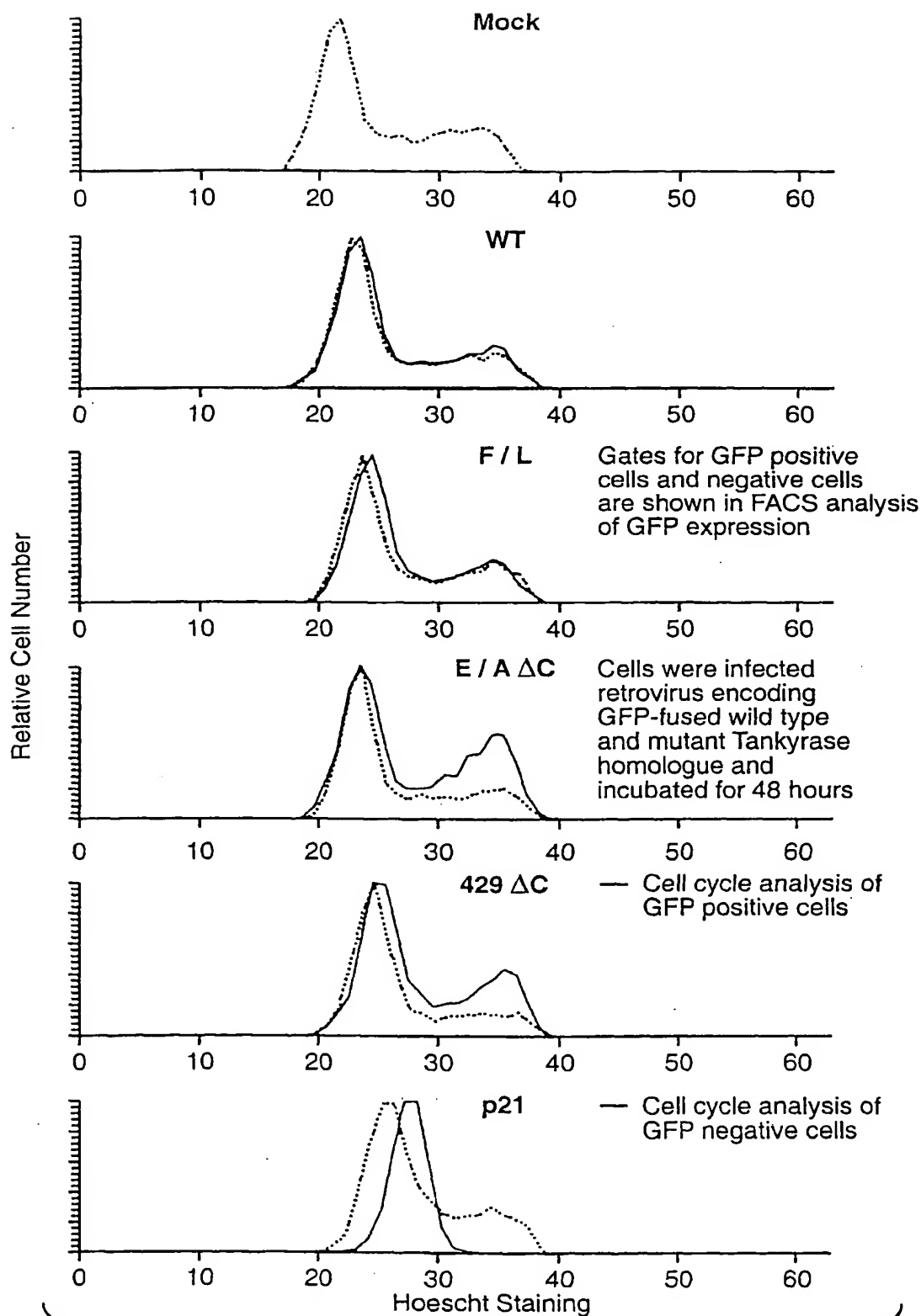
**FIG. 5**

**Cell Cycle Analysis of A549 Cells  
Infected With GFP-fused Wild Type  
and Mutant Tankyrase Homologue**



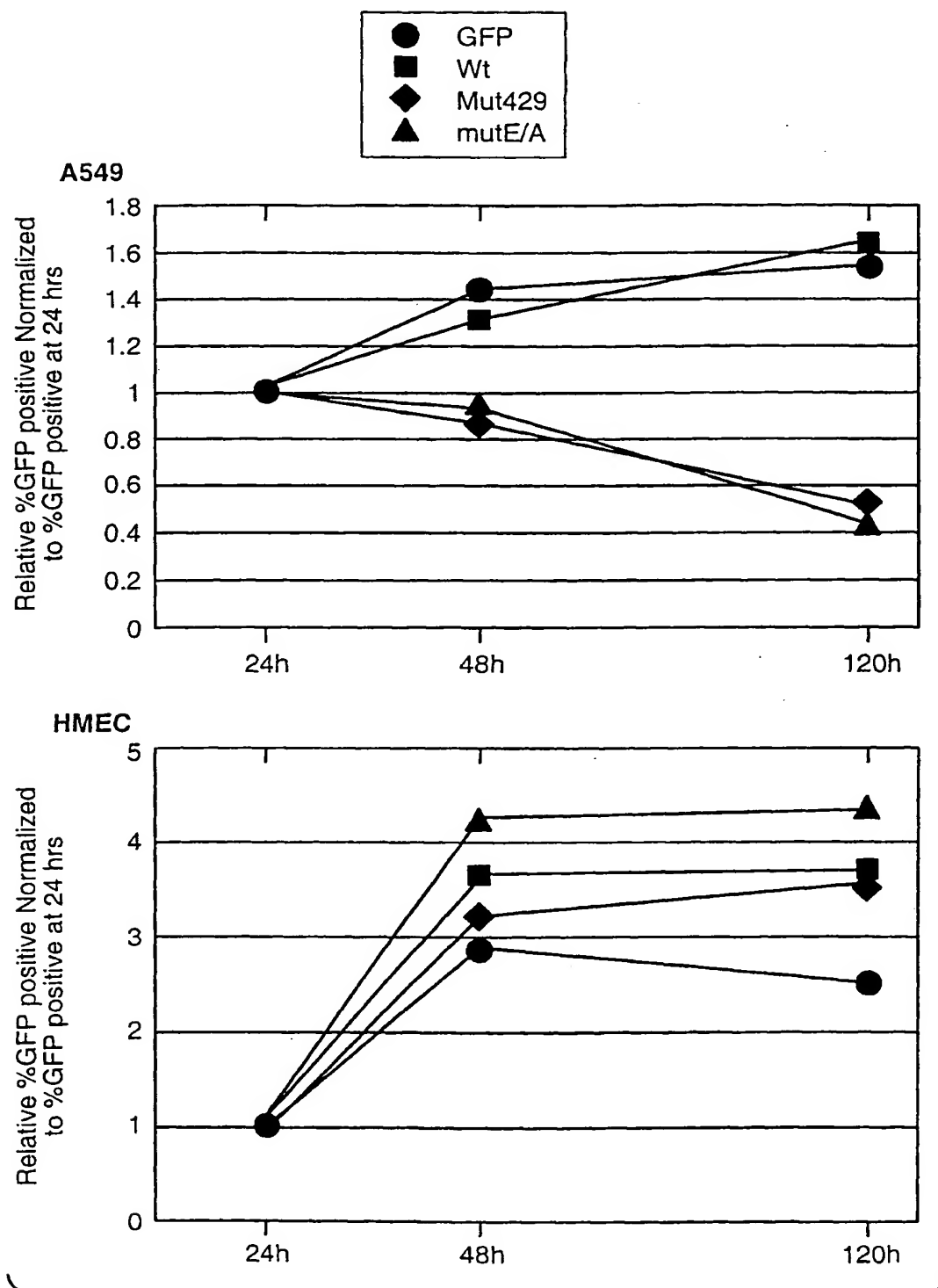
**FIG.\_6A**





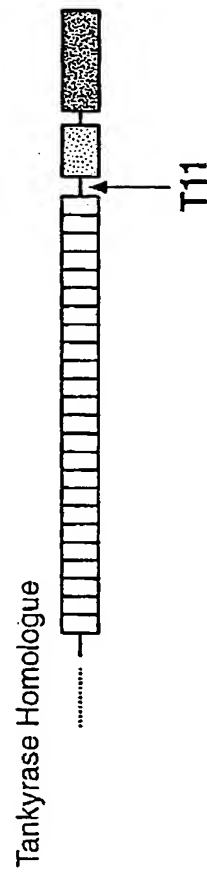
**FIG. 6B**

**Kinetics of GFP Positive cells in A549 Cells and Human Mammary Epithelial Cells (HMEC) After Retrovirus Infection Encoding GFP-fused Wild Type and Mutant Tankyrase Homologue**



**FIG.\_7**

# The Binding Site of Antisense Oligos Against Tankyrase Homologue



□ Ankyrin repeat    ▨ SAM    ▩ PARP

..... Unidentified sequence

T11

	GTGGAACACAGAGGGTGCTTCC	
Tankyrase Homologue	GTGGAACACAGAGGGTGCTTCCAGTTTGAGAAAAAGGAGGTCCAGAGTAGATTTAGCAT	2838
Tankyrase	ATGCAGGGGATGGCGCCCGCGGGAACAGAAAAAGGAAGGAGAGAGTTGCTGGTCTTGACAT	3091
	** *	

FIG.\_8

# Anti-Proliferative Phenotype of Antisense Oligonucleotides Against Tankyrase Homologue in A549 and HeLa Cells

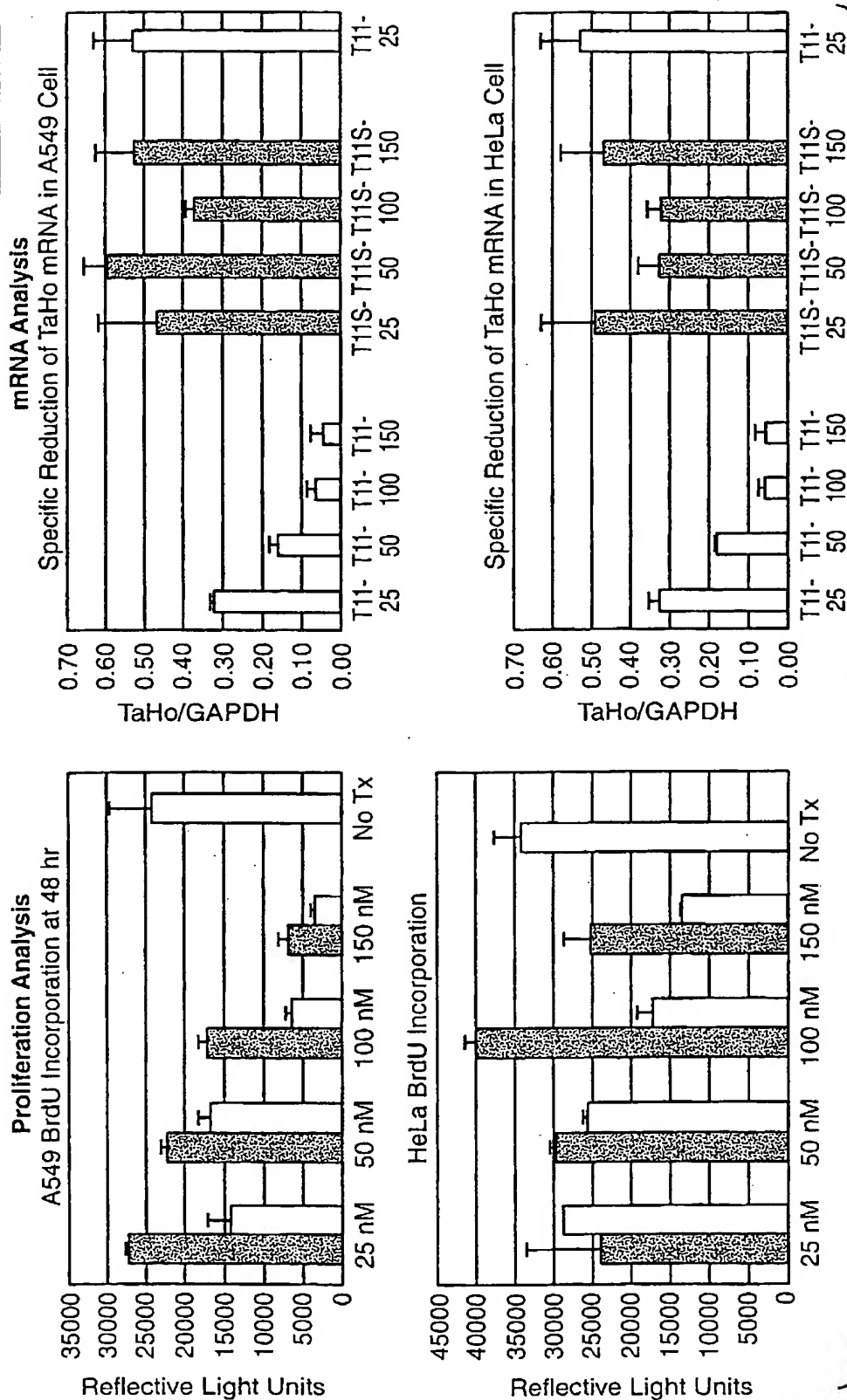
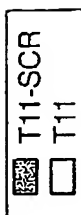
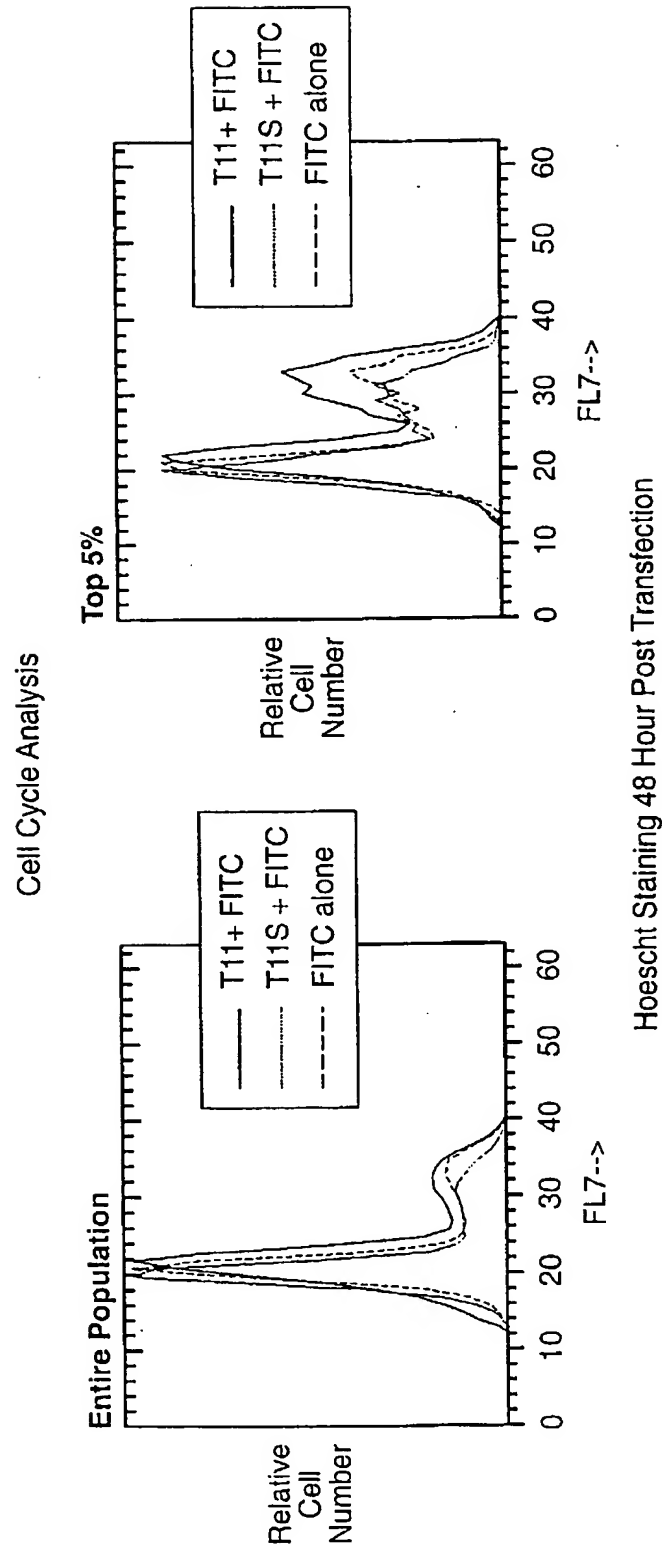


FIG. 9

## Gates for Cell Cycle Analysis



Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC). After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle



**FIG. 10B**

mRNA Expression of Tankyrase Homologue in Several Tumors and Normal Tissues by a Taqman Analysis, mRNA Expression was Normalized by 90kDa Highly Basic Protein (HBP) and Ribosomal Protein S9 (S9)

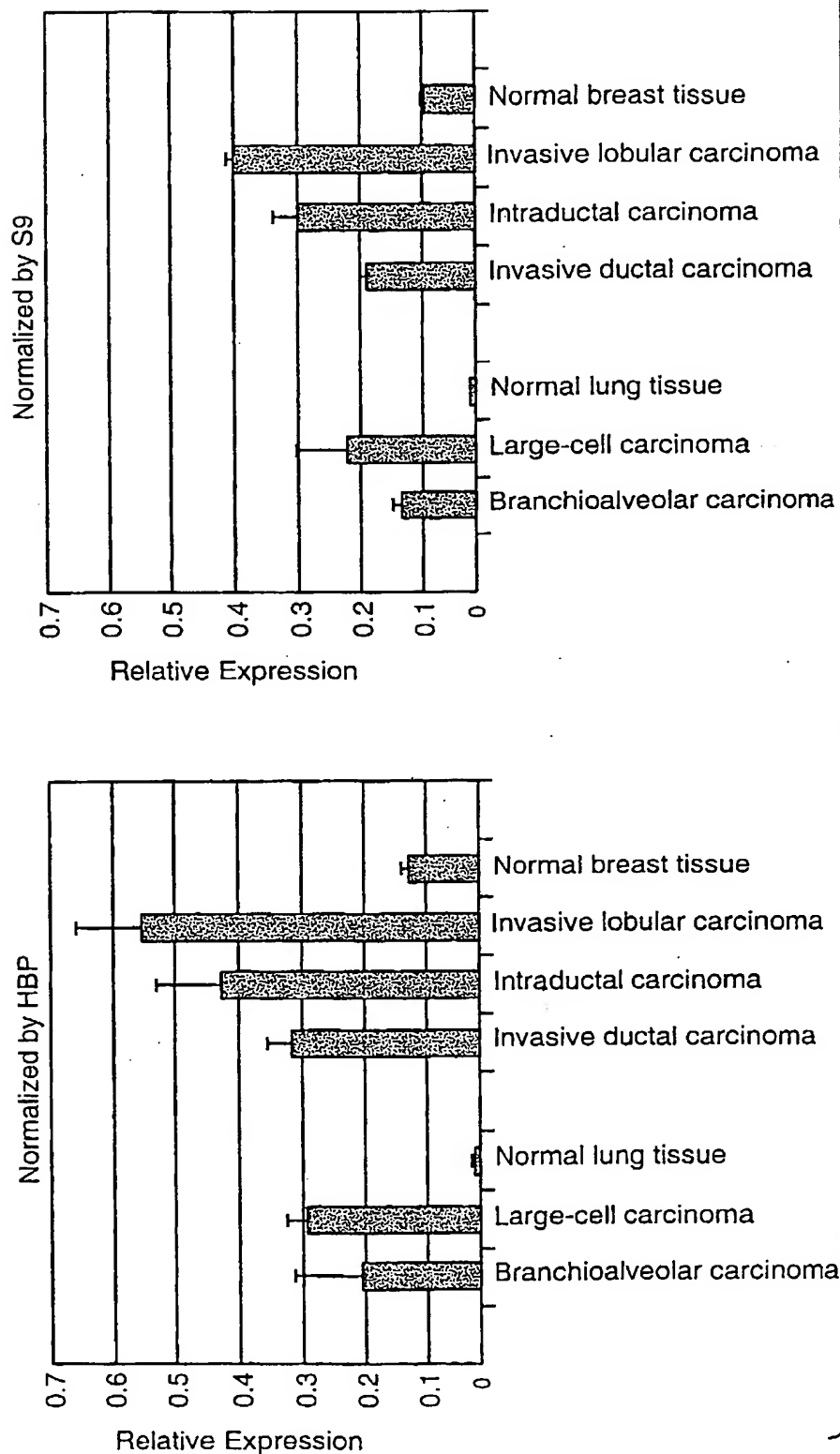


FIG. 11

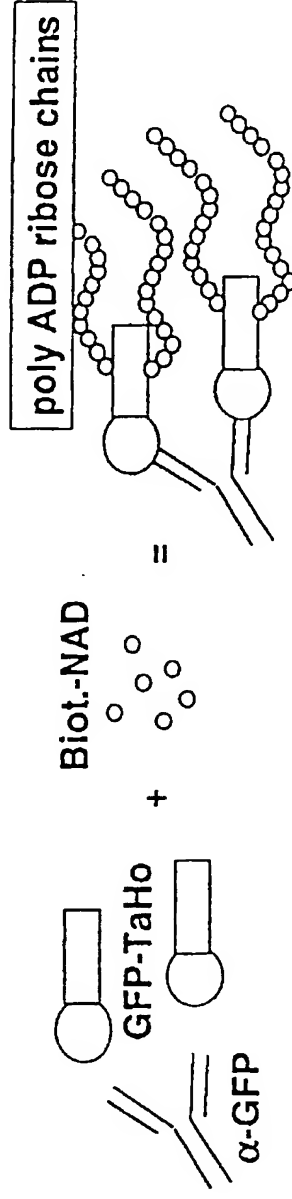
**Procedure for Nonisotopic Detection of Poly-ADP Ribosylation  
Using Anti-GFP mAb-Coated Plates**

Protein lysates from 293T cells normalized by GFP  
fluorescence and total protein

↓  
Immobilization of GFP-tankyrase homologue in anti-  
GFP Coated plates

↓  
Auto PARP reaction with Biotinylated-NAD in 96 wells

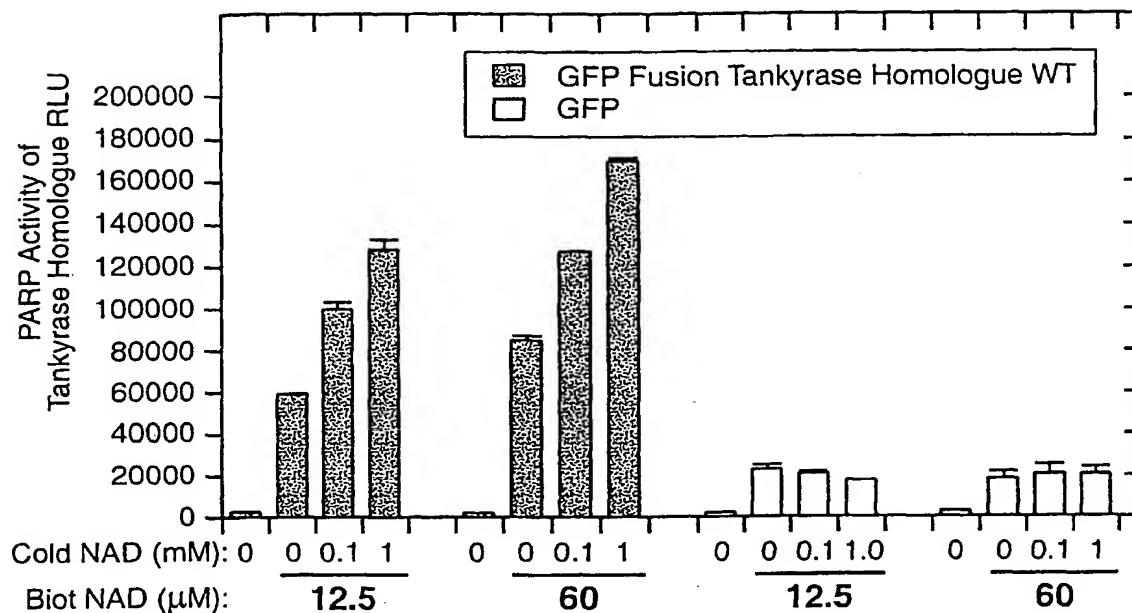
↓  
Detection of poly ADP ribose chains with Streptavidin-  
HRP and chemiluminescent substrate



**FIG.\_12**



**Non-Isotopic Plate-Based Detection of TaHo PARP  
Activity in the Presence of Biotinylated NAD**



**FIG. 13**

**Comparison of IC<sub>50</sub> Values of the PARP Inhibitors**

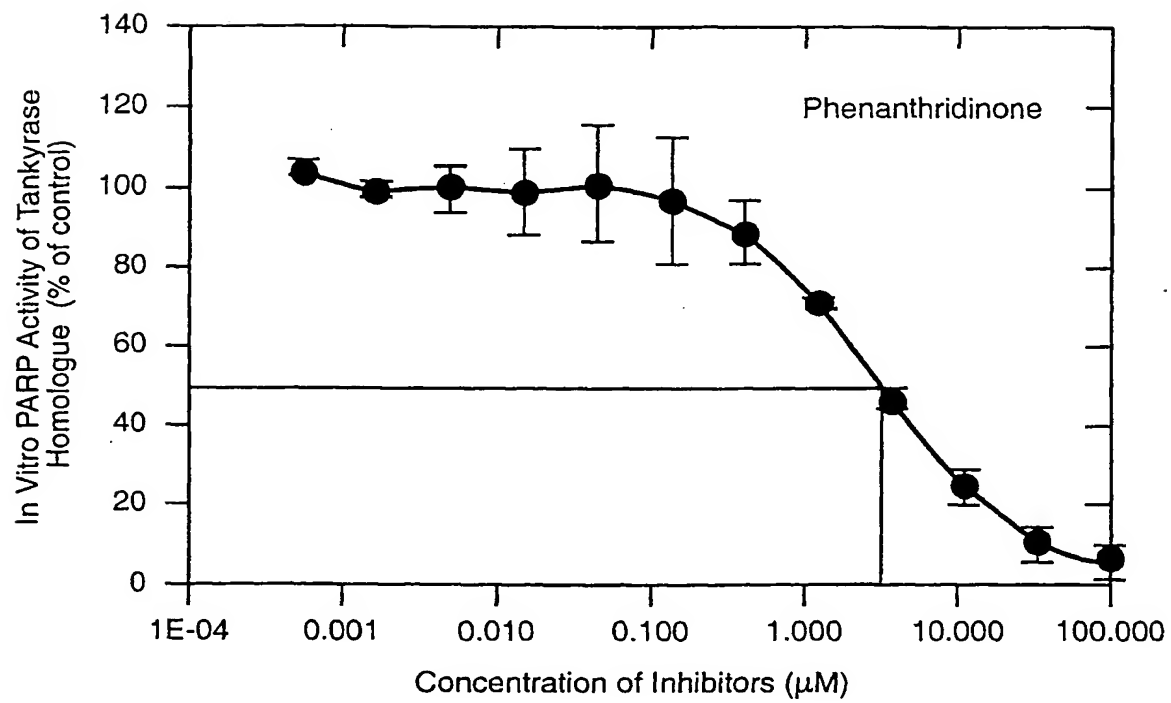
	Approximate IC <sub>50</sub> (nM)	hPARP assay IC <sub>50</sub> (nM)		
	TaHo	Rigel	Decker*	Rankin*
3AB	>50 000	5 000	2 000	5 400
6(5H)Phenanthridinone	1 000-2 000	300		
Niacinamide	>50 000	30 000	>>5 000	31 000

\* Decker P et al., Clinical Cancer Research. 1999 May; 5:1169-1172

\* Rawkin PW et al., J Biol Chem. 1989 Mar 15;264(8):4312-4317

**FIG. 14**

**Inhibition of Tankyrase Homologue PARP Activity  
by hPARP Inhibitors**



***FIG.\_15***

TH-1: Tankyrase Homologue isoform-1, TH-2: Tankyrase Homologue isoform-2 FIG. 16A  
M (Red): the first methionine in the sequence, Z: stop codon  
In this figure, the first methionine in TH-1 sequence is position 1 (M1)

Taho C terminus deletion mutant ends at position 429 (K) and adds 28 amino acids because of frame shift.

Taho F/L mutant has the mutation at position 871

Taho E/A dC mutant has the mutation at position 948, ends at position 957 (A) and adds 2 amino acids.

TH-1	-----	
TH-2	RCSARRGAAGGQGAQRGARVGAAHGTAPDPVTAGSQ	-231
TH-1	-----	
TH-2	AARALSASSPGGLALLAGPGLLLRLLALLAVAAARIMSGRRRCAGGGAACASAAAEAVE	-171
TH-1	-----	
TH-2	PAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHFAAGFGRKDVVEYLLQNGA	-111
	Ankyrin repeat	Ankyrin repeat
TH-1	SVQARDDGGLIPLHNACSFGEVNVNLLLRHGADPNARDNWNYPPLHEAAIKGKIDVCIV	-51
TH-2	NVQARDDGGLIPLHNACSFGEVNVNLLLRHGADPNARDNWNYPPLHEAAIKGKIDVCIV	-51
	Ankyrin repeat	Ankyrin repeat
	•TH1 start	
TH-1	LLQHGAETIRNTDGR TALDADPSAKAVLTGEYKKDELLESARSGNEEKMALLTPLNV	10
TH-2	LLQHGAETIRNTDGR TALDADPSAKAVLTGEYKKDELLESARSGNEEKMALLTPLNV	10

FIG.\_16B

TH-1	_____	_____	_____	_____
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-2	NCHASDGRKSTPLHLAAGYNRKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTEL	70		
	NCHASDGRKSTPLHLAAGYNRKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTEL	70		
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-1	LVKHGACVNAMDLWQFTPLHEAASKNRVECSLLLSYGADPTLLNCHNKS AIDLTPQL	130		
TH-2	LV			
	_____	Ankyrin repeat	_____	_____
TH-1	KERLAYEFKGHSLLOAAREADVTRIKKHLSEMVNFKHPQTHETALHCAA SPYPKRKQI	190		
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-1	CELLLRKGANINEKTKEFLTPLHVASEKAHNDVVEVVVKHEAKVNALDNLGQTS LHRAAY	250		
	_____	Ankyrin repeat	_____	_____
TH-1	CGHLQTCRLLLSYGCDPNIISLQGF TALQMGNE NVQQLQEGISLGNSEADRQLLEAKA	310		
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-1	GDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVEYLLQHGADVHAKDKGGLVP	370		
	_____	Ankyrin repeat	_____	Ankyrin repeat
TH-1	LHNACSYGHYEVAELLVKHGAVVNVADLWKFTPLHEAAAKGYEICKLLLLQHGADPTKKN	430		
	_____	Ankyrin repeat	_____	Ankyrin repeat
				Deletion---
TH-1	GMEILLWILLKMEIQIFKICLGEMQLCZ			
	RDGNTPLDLVKDGDTDIQDLLRGDAALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTP	490		
	_____	Ankyrin repeat	_____	_____

FIG. 16C

TH-1	LHLAAGYNNLEVAEYLLQHGADVNAQDKGLIPLHNAASYGHVDVAALLIKYNACVNDATD 550 Ankyrin repeat Ankyrin repeat
TH-1	KWAFPLHEAAQKRTQLCALLLAHGADPTLKNQEGQTPLDLSADDDVSALLTAAMPSPA 610 Ankyrin repeat Ankyrin repeat
TH-1	LPSCYKPPQVLNGVRSPGATADALSSGSPSPSSLSAASSLDNLGSGFSELSSVSSSGTEG 670 Ankyrin repeat
TH-1	ASSLEKKE--VPGVDFSITQFVRNLGLEHLMDFEFEREQITLDVLVEMGHKELKEIGINAY 730 SAM domain
TH-1	GHRHKLIKVERLISGQQLNPYLTNTSGSGTILIDLSPDDKEFQSVVEEMQSTVREHR 790
TH-1	DGGHAGGIFNRYNLIKQVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFVNAIL 850
TH-1	HKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYIGGGTGCPVHKDRSCYICHRQLLFCR 910 • F→L mutation PARP domain
TH-1	VTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIMRP 970 • E→A • Deletion. -----A-----LSZ
TH-1	EGMVDG 976